



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,617	09/04/2003	Takahiro Fujiwara	59585(71526)	8014
21874	7590	04/27/2005	EXAMINER	
EDWARDS & ANGELL, LLP			NYALLEY, LANSANA	
P.O. BOX 55874			ART UNIT	
BOSTON, MA 02205			PAPER NUMBER	
			1621	

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/656,617	FUJIWARA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Lansana Nyalley	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☐ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☒ Claim(s) 5-7 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____  |

## DETAILED ACTION

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness

or nonobviousness.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bertau et. al.

(Tetrahedron: Asymmetry 12, year 2001, 2103-2107) in combination with Ratovelomanana-

Vidal et. al. (J. Org. Chem. 1996, 568 (1998), 163-171)

### WHAT APPLICANTS CLAIM.

Applicants claim a process for the production of an optically active amino alcohol represented by the following formula (I),

(wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, A<sub>1</sub>, A<sub>2</sub>, m, n and \* have the same meaning which will be defined below where the relative configuration of hydroxyl group to amino group on each of the

asymmetric carbons marked \* is trans) or a salt thereof, comprising reacting an optically active hydroxycarboxylate represented by the following formula (IV),

(wherein, R1 is an alkyl group having 1 to 6 carbon(s); R2 to R5 each independently is hydrogen atom, a lower alkyl group or an optionally-substituted phenyl group; with proviso that R2 and R4 or R2 and R5 or R3 and R4 or R3 and R5, taken together with the carbon atoms to which they are attached optionally form a ring or fused ring; A1 is  $-(CH_2)_m$  while A2 is  $-(CH_2)_n$  (wherein m and n each is an integer of 0 to 3 and  $m + n$  is 1 to 3); and \* is an asymmetric carbon atom where the relative configuration of hydroxyl group to alkoxycarbonyl group on each of the asymmetric carbon marked \* is trans) with hydrazine to prepare an optically-active hydroxycarboxylic hydrazide compound represented by the following formula (III)

(wherein, R2 to R5, A1, A2, m, n and \* have the same meaning as defined above where the relative configuration of hydroxyl group to hydrazinocarbonyl group on each of asymmetric carbons marked \* is trans), then conducting a Curtius reaction in the presence of an alcohol represented by the following formula (VI)

(wherein, R6 is an alkyl group having 1 to 6 carbon(s) or an optionally-substituted benzyl group) to give an optically active alkoxycarbonylamino alcohol represented by the following formula (II)

(wherein, R2 to R5, A1, A2, m, n and \* have the same meanings as defined above where the relative configuration of hydroxyl group to hydrazinocarbonyl group on each of asymmetric carbon marked \* is trans) and then deprotecting a protective group for the amino group.

**DETERMINATION OF THE SCOPE AND THE CONTENT OF THE**

**PRIOR ART (M.P.E.P. 2141.01).**

Bertau et. al. teach a process for the production of a straight chain, optically active 2-amino cyclohexanol using the following steps comprising:

Enantioselective reduction of keto ester in the presence of yeast to form a 2-alkonoate cyclohexanol intermediate; reacting the resulting intermediate with hydrazine in the presence of alcohol such as methanol and ethanol using Curtius degradation method (to preserve the conformation of the substituents) to form a hydrazide intermediate and then deprotecting the amine to produce the final product, a cis-2- amino cyclohexanol (See pages 2103- 2105)

**ASCERTAINMENT OF THE DIFFERENCE BETWEEN THE PRIOR ART  
AND THE CLAIMS (M.P.E.P. 2141.02).**

The difference between Bertau et. al. and the claims in the instant application is that Bertau et. al. do not teach a selective reduction of beta keto ester on cyclohexanone; they do not teach the use of hydrogen over ruthenium catalyst; and they do not teach the specific use of a benzyl alcohol.

Ratovelomanana-Vidal et. al. teach the difference by teaching a method for reducing a beta-keto ester to a trans beta hydroxyl ester by reacting the said beta keto ester with hydrogen in the presence of a ruthenium catalyst and an ethanol solvent. The ketone is reduced in preference to the ester.

**FINDING OF PRIMA FACIE OBVIOUSNESS-RATIONAL AND  
MOTIVATION (M.P.E.P. 2142-2143).**

One of ordinary skill in the art at the time the invention was made would have been motivated to look to the teachings of Bertau et. al. and Ratovelomanana-Vidal et. al. because

Bertau et. al. and Ratovelomanana-Vidal et. al. teach a process for the formation of a trans beta ester cyclohexanol by reducing beta ester cyclohexanone in the presence of hydrogen, ruthenium catalyst and ethanol solvent. (See Ratovelomanana-Vidal et. al., page 168).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have looked to the teachings of Bertau et. al. and Ratovelomanana-Vidal et. al., for a method for producing a trans beta-keto ester because Bertau et. al. and Ratovelomanana-Vidal et. al., base on the above, teach the elements of the claimed invention with sufficient guidance, particularity and with reasonable expectation of success that the invention would be prima facie obvious to one of ordinary skill ( the prior art references teach or suggest all the claim limitations with reasonable expectation of success. See M.P.E.P. 2143).

**Allowable Subject Matter.**

Claims 5-7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

**Reasons for Allowance.**

Claims 5-7 are allowable over Bertau et. al. and Ratovelomanana-Vidal et. al. because claims 5-7 have the further limitation of using benzyl alcohol during the Curtius phase of the reaction whereas Bertau et. al. and Ratovelomanana et. al. use ethanol in the similar reaction.

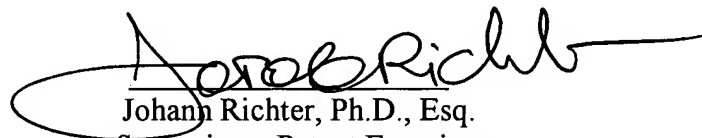
The use of benzyl alcohol in place of ethanol would not have been suggested to one of ordinary skill in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lansana Nyalley whose telephone number is 571,272,0697. The examiner can normally be reached on 7:45 to 4:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571 272 0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300..

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lansana Nyalley, Ph.D.  
03/ 16/ 2005



Johann Richter, Ph.D., Esq.  
Supervisory Patent Examiner,  
Technology Center 1600